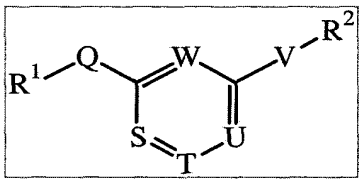
CLAIMS

What is claimed is:

1. A compound of Formula Ia



Ia

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 and R^2 independently are selected from:

Substituted C_1-C_6 alkyl;

Substituted C_2-C_6 alkenyl;

Substituted C_2-C_6 alkynyl;

Substituted C_3-C_6 cycloalkyl;

Substituted C_3-C_6 cycloalkyl-(C_1-C_6 alkylenyl);

Substituted 3- to 6-membered heterocycloalkyl;

Substituted 3- to 6-membered heterocycloalkyl-(C_1-C_6 alkylenyl);

Phenyl-(C_1-C_6 alkylenyl);

Substituted phenyl-(C_1-C_6 alkylenyl);

5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Phenyl;

Substituted phenyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

R^3O-(C_1-C_6 alkylenyl);

Substituted R^3O-(C_1-C_6 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5- or 6-membered heteroaryl;

Substituted 5- or 6-membered heteroaryl;

8- to 10-membered heterobiaryl;

Substituted 8- to 10-membered heterobiaryl;

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl); and

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Each R^3 independently is selected from:

Substituted C_1-C_6 alkyl;

Substituted C_3-C_6 cycloalkyl;

Phenyl-(C_1-C_6 alkylenyl);

Substituted phenyl-(C_1-C_6 alkylenyl);

5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

Phenyl;

Substituted phenyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

S, T, U, and W each are C-R^4; or

One of S, T, U, and W is N and the other three of S, T, U, and W are C-R^4; or

Two of S, T, U, and W are N and the other two of S, T, U, and W are C-R^4; or

T is C-R^4 and S, U, and W are each N; or

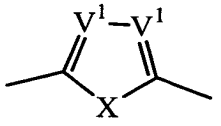
U is C-R^4 and S, T, and W are each N; or

S is C-R^4 and T, U, and W are each N;

Each R^4 independently is selected from: H, F, CH_3, CF_3, C(O)H, CN, HO, CH_3O, $C(F)H_2O$, $C(H)F_2O$, and CF_3O;

V is a 5-membered heteroarylenyl; and

Q is selected from: OCH_2, $N(R^6)CH_2$, $OC(O)$, $CH(R^6)C(O)$, $OC(NR^6)$, $CH(R^6)C(NR^6)$, $N(R^6)C(O)$, $N(R^6)C(S)$, $N(R^6)C(NR^6)$, $N(R^6)CH_2$, $SC(O)$, $CH(R^6)C(S)$, $SC(NR^6)$, trans-(H)C=C(H), cis-(H)C=C(H), C≡C, $CH_2C{\equiv}C$, $C{\equiv}CCH_2$, $CF_2C{\equiv}C$, $C{\equiv}CCF_2$,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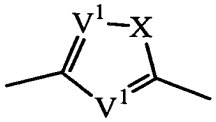
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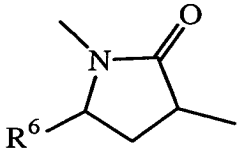
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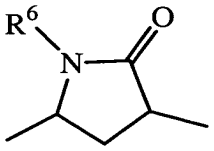
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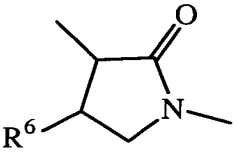
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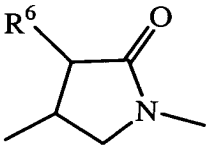
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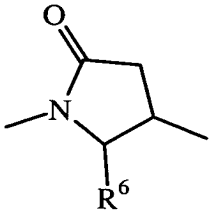
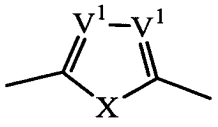

;

or

V is C(O)O, C(S)O, $C(O)N(R^5)$, or $C(S)N(R^5)$; and

Q is selected from: OCH_2, $N(R^6)CH_2$, $CH(R^6)C(O)$, $OC(NR^6)$, $CH(R^6)C(NR^6)$, $N(R^6)C(NR^6)$, $N(R^6)CH_2$, $CH(R^6)C(S)$, $SC(NR^6)$, trans-(H)C=C(H), cis-(H)C=C(H), $C{\equiv}CCH_2$, $C{\equiv}CCF_2$,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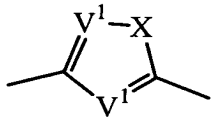
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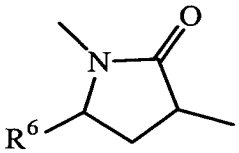
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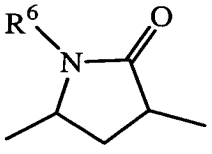
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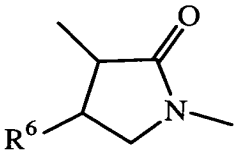
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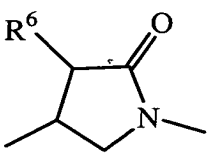
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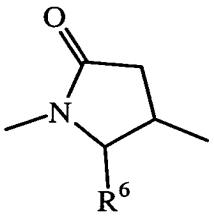

;

R^5 is H or C_1-C_6 alkyl;

R^6 is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N(C_1-C_6 alkyl);

Each V^1 is independently C(H) or N;

Each "substituted" group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

C_2-C_6 alkenyl;

C_2-C_6 alkynyl;

C_3-C_6 cycloalkyl;

C_3-C_6 cycloalkylmethyl;

Phenyl;

Phenylmethyl;

3- to 6-membered heterocycloalkyl;

3- to 6-membered heterocycloalkylmethyl;

cyano;

CF_3;

(C_1-C_6 alkyl)-OC(O);

$HOCH_2$;

(C_1-C_6 alkyl)-OCH_2;

H_2NCH_2;

(C_1-C_6 alkyl)-N(H)CH_2;

(C_1-C_6 alkyl)$_2$-NCH_2;

N(H)$_2$C(O);

(C_1-C_6 alkyl)-N(H)C(O);

(C_1-C_6 alkyl)$_2$-NC(O);

N(H)$_2$C(O)N(H);

(C_1-C_6 alkyl)-N(H)C(O)N(H);

N(H)$_2$C(O)N(C_1-C_6 alkyl);

(C_1-C_6 alkyl)-N(H)C(O)N(C_1-C_6 alkyl);

(C_1-C_6 alkyl)$_2$-NC(O)N(H);

(C_1-C_6 alkyl)$_2$-NC(O)N(C_1-C_6 alkyl);

$N(H)_2C(O)O$;

$(C_1$-C_6 alkyl)-$N(H)C(O)O$;

$(C_1$-C_6 alkyl)$_2$-$NC(O)O$;

HO;

$(C_1$-C_6 alkyl)-O;

CF_3O;

$CF_2(H)O$;

$CF(H)_2O$;

H_2N;

$(C_1$-C_6 alkyl)-N(H);

$(C_1$-C_6 alkyl)$_2$-N;

O_2N;

$(C_1$-C_6 alkyl)-S;

$(C_1$-C_6 alkyl)-S(O);

$(C_1$-C_6 alkyl)-$S(O)_2$;

$(C_1$-C_6 alkyl)$_2$-$NS(O)_2$;

$(C_1$-C_6 alkyl)-$S(O)_2$-N(H)-C(O)-$(C_1$-C_8 alkylenyl)$_m$;

$(C_1$-C_6 alkyl)-C(O)-N(H)-$S(O)_2$-$(C_1$-C_8 alkylenyl)$_m$;

HO-C(=O)-$(C_1$-C_3 alkylenyl);

HO-C(=O)-$(C_3$-C_6 cycloalkylen-1-yl);

Phenyl substituted with 1 or two substituents selected from F, Cl, OH, OCH_3, C≡N, COOH, $COOCH_3$, $C(=O)CH_3$, and CF_3;

5- or 6-membered heteroaryl;

5- or 6-membered heteroaryl substituted with 1 substituent selected from F, Cl, OH, OCH_3, C≡N, COOH, $COOCH_3$, $C(=O)CH_3$, and CF_3;

SO_3H;

PO_3H_2; and

R^7R^{7a}-$(J)_m$-$N(H)CH_2$, wherein m is an integer of 0 or 1; J is N-C(=O); and R^7 and R^{7a} are independently selected from hydrogen, C_1-C_6 alkyl, (C_1-C_6 alkyl)-C(=O), C_1-C_6 alkyl substituted with 1 or 2 OH, C_1-C_3 alkyl-O-(C_1-C_3 alkylenyl), 5- or 6-membered heteroaryl-C(=O), and (C_1-C_6 alkyl)-$S(O)_2$; or R^7 and R^{7a} may be taken together with the nitrogen atom to

which they are both bonded to form (i) a 3- to 6-membered heterocycloalkyl, optionally substituted with a CH_3 or oxo (i.e., =O), containing the nitrogen atom, 0 or 1 O or S atoms, and carbon atoms or (ii) a 5- or 6-membered heteroaryl containing the nitrogen atom, 0 or 1 additional N atom, and carbon atoms;

wherein each substituent on a carbon atom may further be independently selected from:

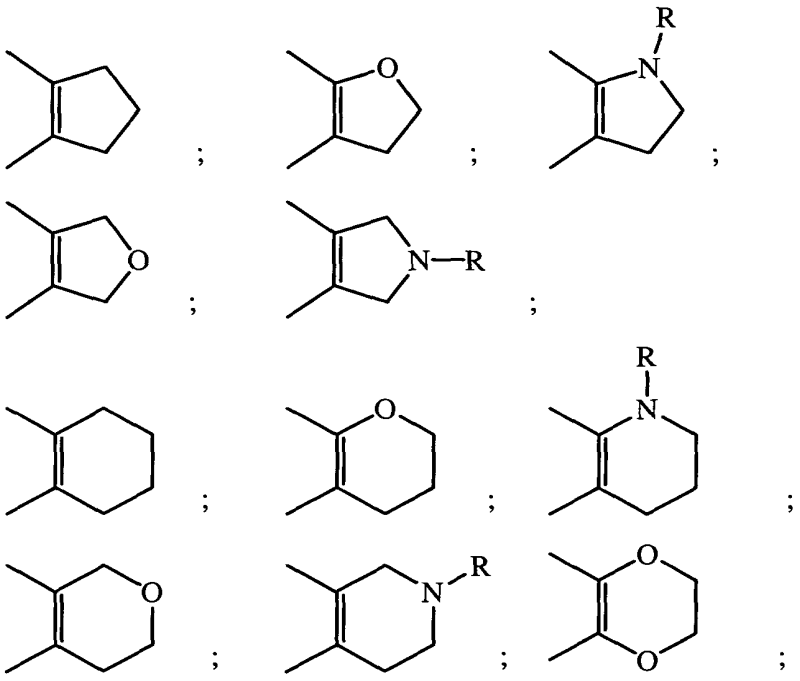
Halo;

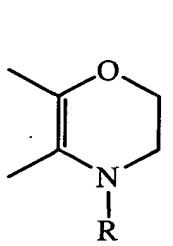
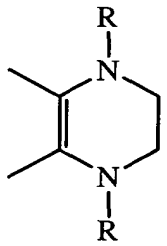
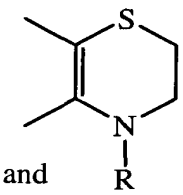
HO_2C; and

OCH_2O, wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



; ; and ;

R is H or C_1-C_6 alkyl;

m is an integer of 0 or 1;

wherein each 5-membered heteroarylenyl independently is a 5-membered ring containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C_1-C_6 alkyl), and 4 N, wherein the O and S atoms are not both present, and wherein the heteroarylenyl may optionally be unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

wherein each heterocycloalkyl is a ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 2 N(H), and 2 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C_1-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings; and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

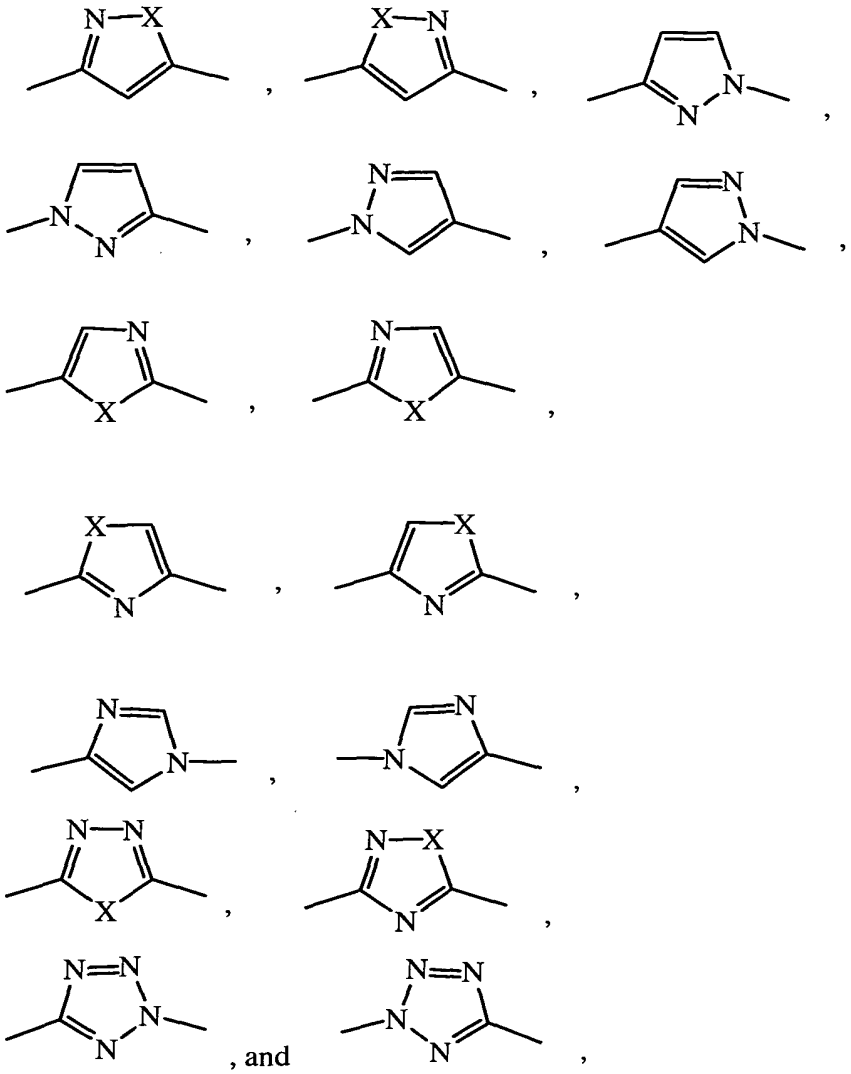
wherein with any (C_1-C_6 alkyl)$_2$-N group, the C_1-C_6 alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein S, T, U, and W are each CH

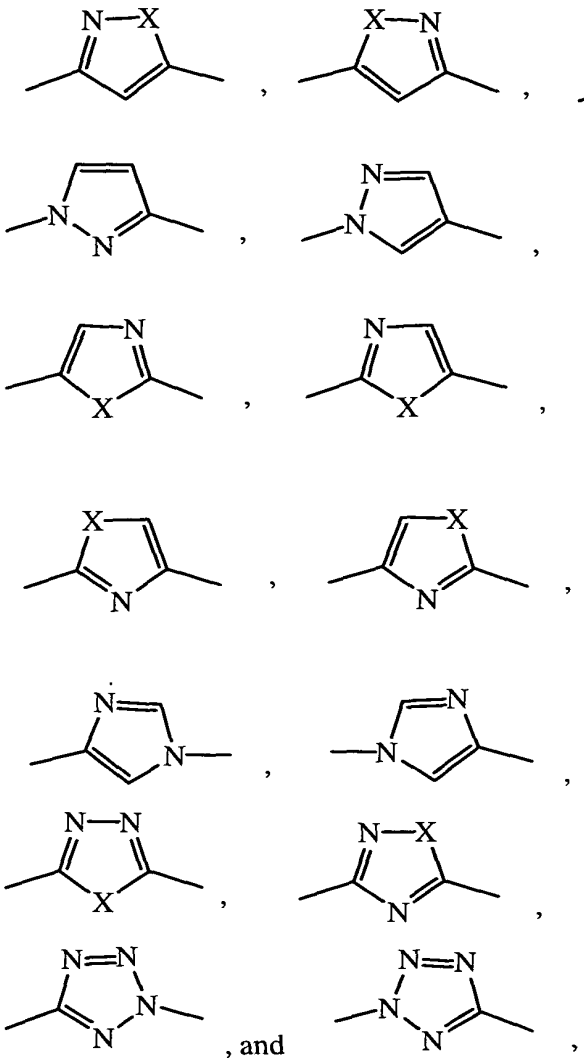
3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein one of S, T, U, and W is N and the other three of S, T, U, and W are each CH

4. The compound according to Claim 2, wherein V is selected from the groups:



wherein X is O, S, or N(H).

5. The compound according to Claim 3, wherein V is selected from the groups:



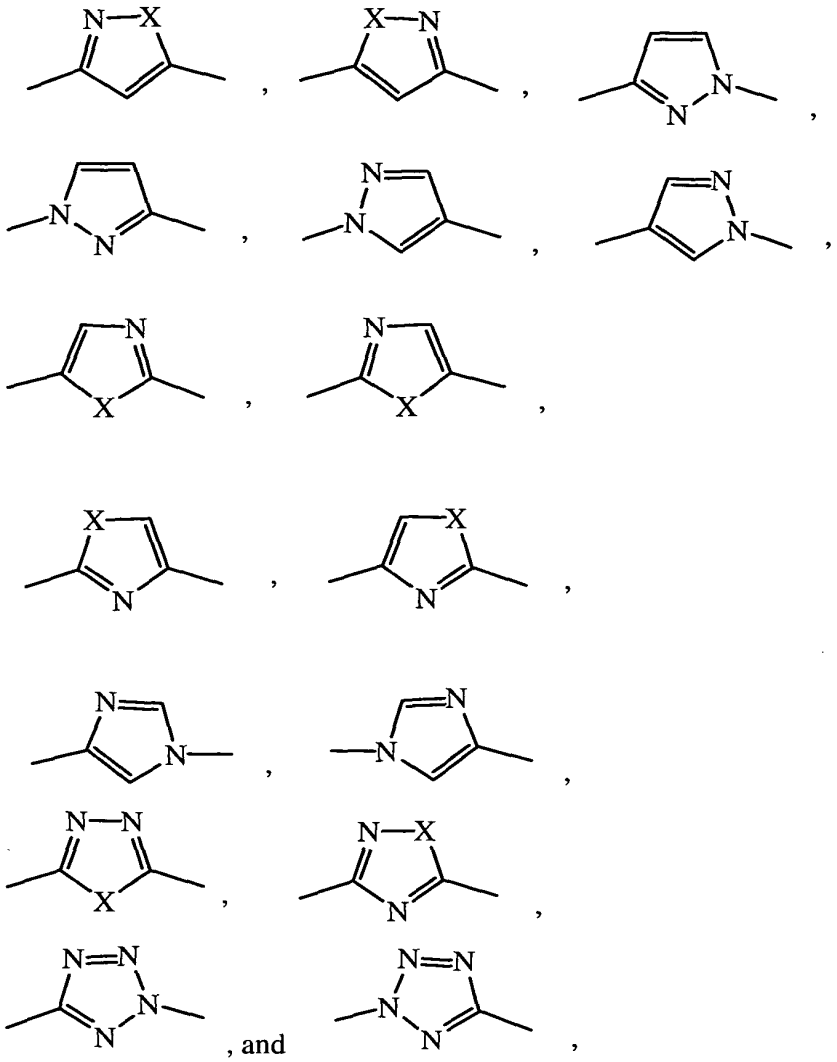
, and

wherein X is O, S, or N(H).

6. The compound according to Claim 4, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C or $N(R^6)C(O)$.

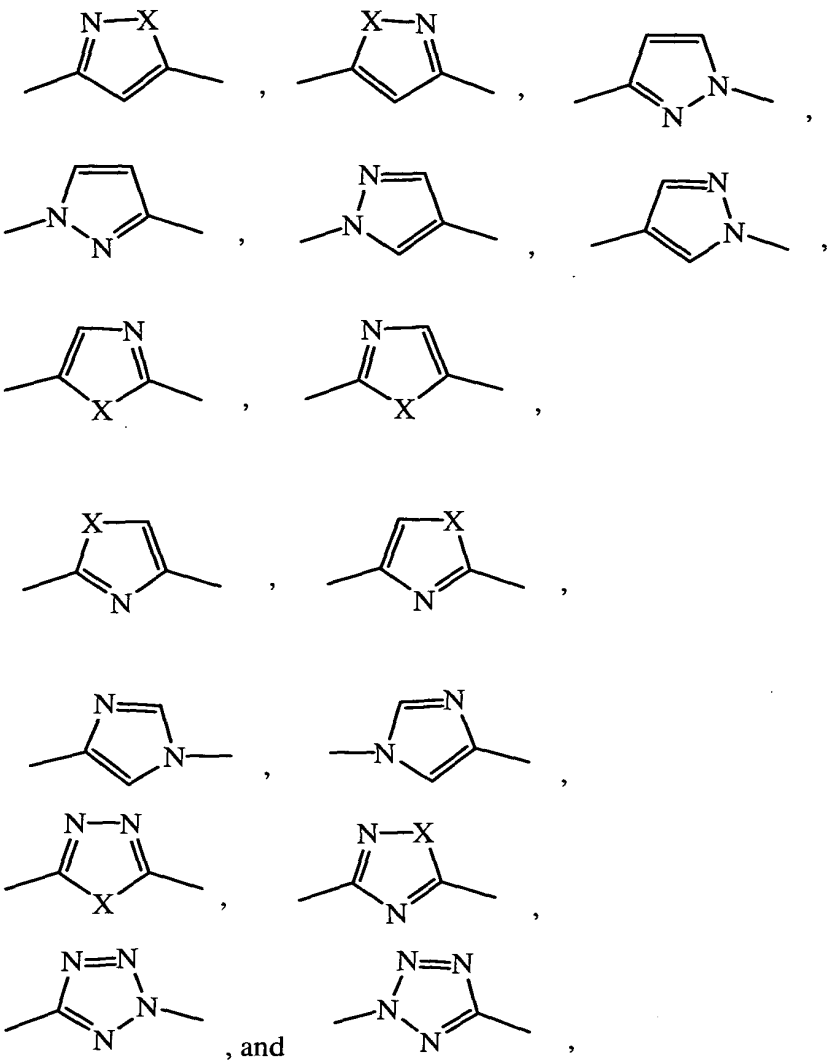
7. The compound according to Claim 5, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C or $N(R^6)C(O)$.

8. The compound according to Claim 4, or a pharmaceutically acceptable salt thereof, wherein Q is selected from:



wherein X is O, S, or N(H).

9. The compound according to Claim 5, or a pharmaceutically acceptable salt thereof, wherein Q is selected from:



wherein X is O, S, or N(H).

10. The compound according to any one of Claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein each of R^1 and R^2 are independently selected from:

Substituted C_3-C_6 cycloalkyl-(C_1-C_6 alkylenyl);

Phenyl-(C_1-C_6 alkylenyl);

Substituted phenyl-(C_1-C_6 alkylenyl);

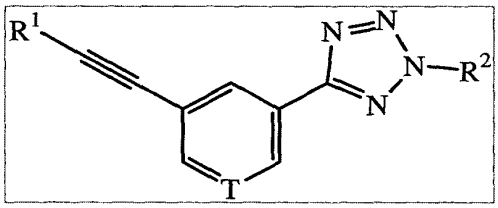
5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl); and

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

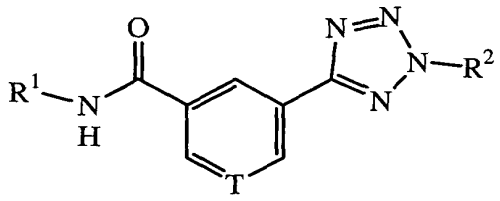
wherein each heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and 5- and 6-membered heteroaryl are monocyclic rings and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other; and

wherein each group and each substituent is independently selected.

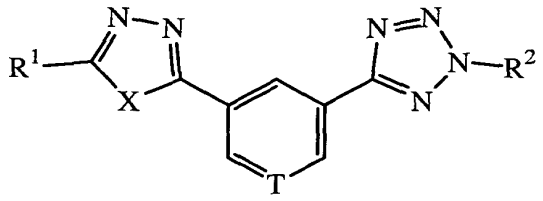
11. The compound according to Claim 1 of Formulas IIa, III, IV, V, VI, VII, or VIII



IIa



III



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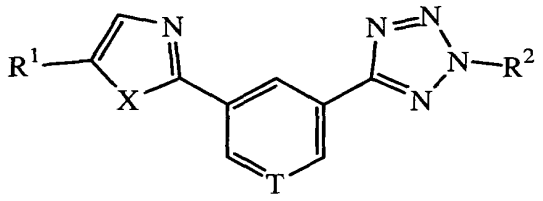

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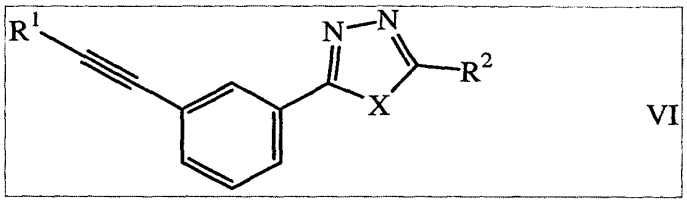

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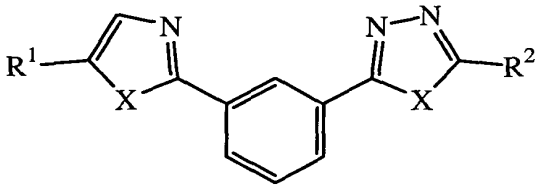
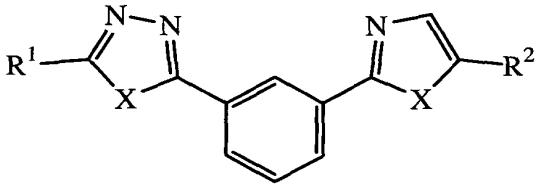


VII



VIII

or a pharmaceutically acceptable salt thereof,

wherein T is CH or N, X is O, S, or N(H), and and each of R^1 and R^2 are independently selected from:

Substituted C_3-C_6 cycloalkyl-(C_1-C_6 alkylenyl);

Phenyl-(C_1-C_6 alkylenyl);

Substituted phenyl-(C_1-C_6 alkylenyl);

5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl); and

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C_1-C_6 alkylenyl);

wherein each heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and 5- and 6-membered heteroaryl are monocyclic rings and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other; and

wherein each group and each substituent is independently selected.

12. The compound according to Claim 1 selected from:

4-(5-{3-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-phenyl}-tetrazol-2-ylmethyl)-benzoic acid;

4-(5-{5-[3-(4-Methoxy-phenyl)-prop-1-ynyl]-pyridin-3-yl}-tetrazol-2-ylmethyl)-benzoic acid;

[4-(5-{3-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-phenyl}-tetrazol-2-ylmethyl)-phenyl]-acetic acid;

4-(5-{3-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-phenyl}-[1,3,4]thiadiazol-2-ylmethyl)-benzoic acid;

4-{5-[2-(4-Fluoro-benzylcarbamoyl)-pyridin-4-yl]-tetrazol-2-ylmethyl}-benzoic acid; and

4-(5-{3-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-phenyl}-tetrazol-2-ylmethyl)-cyclohexanecarboxylic acid;

1-[4-(5-{3-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-phenyl}-tetrazol-2-ylmethyl)-phenyl]-cyclopropanecarboxylic acid;

3-(5-{3-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-phenyl}-tetrazol-2-ylmethyl)-benzoic acid; and

4-{5-[2-(4-Fluoro-benzylcarbamoyl)-6-methyl-pyridin-4-yl]-tetrazol-2-ylmethyl}-benzoic acid; or

a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

14. The pharmaceutical composition according to Claim 13, comprising a compound according to Claim 12, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

15. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

16. The method according to Claim 15, wherein the compound administered is a compound according to Claim 12, or a pharmaceutically acceptable salt thereof.

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